UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/740,211	12/18/2000	Linda B. Couto	AVIGEN.003C1	4340

20995 7590 01/17/2002

KNOBBE MARTENS OLSON & BEAR LLP
620 NEWPORT CENTER DRIVE
SIXTEENTH FLOOR
NEWPORT BEACH, CA 92660

EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1633	8

DATE MAILED: 01/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/740,211	Applicant(s) COUTO ET AL.	
	Examiner Brian Whiteman	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-19* is/are pending in the application.

4a) Of the above claim(s) *2-7 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Applicants petition filed on 1/4/02 paper no. 7 to make special under MPEP 708.02 is acknowledged.

Cancellation of claim 1 and addition of claims 2-19 in paper no. 2 filed on 4/21/01 are acknowledged.

Priority

Applicants claim to priority to 09/470618, 09/364,862, 60/125,974, and 60/104,994 is acknowledged.

Information Disclosure Statement

The information disclosure statement filed on 4/21/01 in paper no. 4 does not fully comply with the requirements of 37 CFR 1.98 because: applicant does not properly cite a patent document listed on the 1449. The date of patent no. 5,255,347 on page 6 should read 7/6/93.

The examiner has considered the references, but in order to have the patent document initialed and dated on the 1449, a new 1449 properly citing the patent must be filed with the response to this office action. Failure to comply with this notice will result in the above mentioned information disclosure statement being placed in the application file with the non-complying information not being considered. See 37 CFR 1.97(i).

Election/Restrictions

Applicants elect group II (claims 8-17 and 19) in paper no. 6 filed on 1/4/02 is acknowledged.

Claim 1-7 and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6.

Claims 8-17 and 19 are pending examination.

Double Patenting

The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 8-15 and 19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 1, 5, and 11-13 of U.S. Patent No. 6,200,560 or claims 1, 5, and 11-13 of US Patent No. 6,221,349. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims of patent '560 are drawn to a method of treating hemophilia in a human comprising providing recombinant adeno-associated virions (AAV) comprising a nucleotide sequence encoding Factor VIII operably linked to expression control elements, wherein the

control elements comprise a liver specific promoter ('560, claims 1 and 5). In addition, the claims are drawn to the method described above, wherein said nucleotide sequence encoding factor VIII comprises a light chain and a heavy chain, wherein said nucleotide sequence is either SEQ ID NO: 13 and SEQ ID NO: 14 and wherein light chain and heavy chain are operably linked by junction, wherein the junction either has the amino acid sequence Ser-Phe or Ser-Phe-Ser-Gln-Asn-Pro-Pro-Val-Leu-Lys-Arg-His-Gln (SEQ ID NO: 15 in the instant application) ('560, claims 11-13).

The claims of patent '349 are drawn to a method of delivering a nucleotide sequence encoding Factor VIII to a mammal comprising: providing recombinant adeno-associated virions (AAV) comprising a nucleotide sequence encoding Factor VIII operably linked to expression control elements, wherein the control elements comprise a liver specific promoter ('349, claims 1 and 5). In addition, the claims are drawn to the method described above, wherein said nucleotide sequence encoding factor VIII comprises a light chain and a heavy chain, wherein said nucleotide sequence is either SEQ ID NO: 13 and SEQ ID NO: 14 and wherein light chain and heavy chain are operably linked by junction, wherein the junction either has the amino acid sequence Ser-Phe or Ser-Phe-Ser-Gln-Asn-Pro-Pro-Val-Leu-Lys-Arg-His-Gln ('349, claims 11-13).

Although the conflicting claims in the instant application, patent '349, and patent '560 are not identical, they are not patentably distinct from each other because each invention encompasses the same material and the patents use the pharmaceutical composition encompassed in the instant application. The difference between the claims of the instant application and patent '560 and patent '349 is that the application encompasses the pharmaceutical composition that is

used in the method for treating hemophilia in a human of patent '560 or delivering a nucleotide sequence encoding Factor VIII to a mammal of patent '349. Therefore, the claims of the instant application, patent '560, and '349 are obvious variants of one another.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8, 9, 10, 16, 17, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chiorini et al. (US Patent No. 5,693,531) taken with Simonet (US Patent No. 6,268,212, filed on 1994). Chiorini teaches an AAV vector and AAV particles generated therefrom (column 1, lines 4-5 and column 8, claim 1). The vector system for producing a virus particle (virion) comprises a vector being an AAV vector, including the 5' and 3' ITRs and a heterologous sequence (column 8, claim 1). Chiorini further teaches that the DNA sequence may encode Factor VIII and be under control of a suitable promoter (column 3, lines 5-30). Chiorini does not specifically teach using a pharmaceutical composition (e.g. water) comprising the virion described above, however, it would have been obvious to one of ordinary skill in the art that the virion was contained in a pharmaceutical composition because it is well known in the art that when using virions in an experiment, they are stored in sterile water. However, Chiorini does not teach a pharmaceutical composition comprising a recombinant AAV virion comprising a human Factor VIII subunit operably linked to a tissue specific promoter [e.g. liver-specific, HNF-3 albumin promoter or the transthyretin (TTR) gene promoter].

However, at the time the invention was made, tissue specific promoter, specifically liver-specific promoters (e.g. TTR) were well known in the art for use in enhancing liver expression of a transgene using a vector as exemplified by Simonet. Simonet teaches several liver-specific promoters (e.g. albumin or TTR) that could be used in producing a vector comprising a transgene (expressed in the liver) operably linked to a liver-specific promoter (column 3, line 64-column 4, line 12 and abstract).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention made as routine to combine the teaching of Chiorini and Simonet to make a

pharmaceutical composition comprising a recombinant AAV comprising a human Factor VIII subunit operably linked to a liver specific promoter (e.g. HNF-3 albumin or TTR promoter). One of ordinary skill in the art would have motivated to make the composition because factor VIII is expressed in the liver and it is routine practice to one of ordinary skill in the art to use tissue specific promoters to increase gene expression of a vector in the tissue of interest as taught by Simonet.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ms. Tracey Johnson whose telephone number is (703) 305-2982. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, primary examiner, Dave Nguyen can be reached at (703) 305-2024.

If attempts to reach the primary examiner by telephone are unsuccessful, the examiner's supervisor, Debbie Clark can be reached at (703) 305-4051.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1633
January 11, 2001

DAVE T. NGUYEN
PRIMARY EXAMINER